Internal jugular vein morphology and hemodynamics in patients with multiple sclerosis

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Aim. The aim of this study is to compare the hemodynamics and the morphology of the internal jugular veins using Colour-Doppler and B-mode sonography in multiple sclerosis patients (MS) and in controls.

Methods. The internal jugular veins of 25 MS patients and 25 controls were examined using colour Doppler and B-mode ultrasound in sitting and supine positions, recording the changes in hemodynamics and the presence or absence of morphological changes. The presence of at least two of the extracranial Zamboni criteria in the same individual was considered positive for evidence of chronic cerebrospinal venous insufficiency (CCSVI).

Results. According to the described criteria, 92% of the MS patients showed abnormal findings and 84% of them showed evidence of CCSVI, however; only 24% of controls showed abnormal findings, but none of them showed evidence of CCSVI (OR=7.25, 95% CI 2.92-18.01, P<0.0001).

Conclusion. Hemodynamic abnormalities and morphological changes involving the internal jugular vein are strongly associated with MS. These findings can be demonstrated by a non-invasive, cost effective Doppler ultrasound criteria.

Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system. Recent studies have suggested that MS is highly associated with a condition known as chronic cerebrospinal venous insufficiency (CCSVI) which is only seen in MS patients and not in patients who suffer neither from other neurodegenerative disorders nor in healthy individuals.1, 2 CCSVI is a condition which is recently described and characterized by multiple areas of stenosis of the extracranial venous draining pathways,3 namely the internal jugular veins and the Azygus veins, with collateral formation.4 The normal venous drainage pathway of the blood leaving the brain is via the internal jugular veins and the vertebral veins; the former is favored in the supine posture and the latter in the upright position. The Azygus vein is the main route for venous drainage of the spinal cord.1, 2 CCSVI can be easily assessed using Doppler sonography,1, 2, 5 by evaluating the extracerebral venous hemodynamics with changes in posture, and to assess the morphology of the venous system in patients with MS. The aim of this paper is to compare the hemodynamics and morphology of the jugular veins using Colour-Doppler and B-mode sonography in MS patients and in controls.

Materials and methods

This is a sample for an ongoing study. We are still recruiting more patients and controls. This study was approved by Institutional Review Board (IRB) at Jordan University of Science and Technology. Patients were self referred, controls were recruited from hospital staff or from patient referred for other unrelated ultrasound examinations. Twenty five patients (female: male 13:12), with clinically proven MS according to modified McDonald criteria 6 and 25 healthy age and gender matched controls underwent ultrasound for the internal jugular veins (Table I). Twenty-one patients (84%) were relapsing remitting MS and 4 patients (16%) were secondary progressive MS. Non of the examined patients were primary progressive MS. The examination was performed using a high frequency probe (4-7 MHz) using

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high resolution ultrasound machine (ATL, HDI 5000, USA) with the patients in the sitting and supine positions. In some patient high frequency small curved probe (5-8 MHz) was used, we found this probe is particularly helpful for visualization of brachiocephalic trunk. The study we performed was not blinded. Special attention was made for the presence of the following parameters extracranial Zamboni criteria: 1, 3 1) reflux in IJV in sitting and supine positions. Reflux was considered significant when persistent for more than 0.88 seconds.(1, 5) Reflux in the deep cerebral veins (DCVs) was not assessed due to the lack of the required ultrasound probe in our institution. 2) High resolution B-mode evidence of stenosis or morphological abnormality of IJV. This includes the presence of frank proximal IJV stenosis, abnormal valve, intraluminal septum, flap or diaphragm and ectasia of the carotid bulb causing persistent significant compression on the mid IJV. Narrowing at this area was considered significant when it was associated with flow disturbances, more than 50% narrowing or extensive collateral circulations. 3) Flow not Doppler detectable in the IJVs. 4) Reverted postural control of the main cerebral venous outflow pathway. Negative change in cross sectional area (CSA) of IJV. CSA was measured in both sitting and supine position. Change of CSA was measured by subtracting CSA in supine from CSA in sitting position. Negative result was considered abnormal. We assumed the presence of at least two of the parameters in the same individual positive for evidence of CCSVI. 1, 3

Results

According to the described criteria; 92% of the MS patients showed abnormal findings, and 84% of the patients showed evidence of chronic cerebrospinal venous insufficiency, however; only 24% of controls showed abnormal findings, and none of them showed evidence of CCSVI (Table II). The risk of MS increased of over 7 folds in the presence of positive extracranial Zamboni criteria (OR=7.2, 95% CI 2.9-18, P<0.0001, Table III). The commonest finding was the presence of persistent reflux in the IJV, demonstrated by similar colour flow as in the common carotid artery with negative Doppler flow that was persistent for more than 0.88 seconds (Figure 1). Anomalous morphology of the internal jugular vein was noted, including frank stenosis (8%), presence of a flap within the lumen of the vein in 24% of cases which caused turbulent flow (Figure 2). In one young patient (16 years) a flap was seen in both IJVs. Also, a flap was
seen at the brachiocephalic/ internal jugular vein junction in 20% of patients (Figure 3), this finding was described previously by Zamboni et al. in selective venography. Abnormal valve leaflets were seen in 8%, the abnormality included a reversed orientation of one leaflet, and in another patient one of the leaflets appeared thickened and fixed in a transverse direction causing severe flow disturbances (Figure 4). In 12%; an echogenic membrane was seen to cause significant narrowing of the vein lumen with turbulent flow. In 20% of patients an ectatic carotid bulb causing severe narrowing of the mid part of the IJV with apparent reflux flow was noted (Figure 5). An interesting observation in our study regarding most of these findings; was that the abnormalities were seen more common on the left side than on the right side (Figure 6). In two relapsing remitting MS patients; no venous morphological or hemodynamic abnormalities were detected. In the 25 controls, only 24% of them were positive for a single parameter which was reflux.

Statistical analysis

Age was described using mean (SD) and median. Other variables were described using percentages. The difference in the percentages of abnormalities between MS patients and controls were analysed using Fisher’s Exact test and Chi square whenever appropriate.

Data were analysed using Statistical Package for the Social Sciences SPSS. The two-sided Fisher exact test followed by the determination of odds ratio (95% CI) was used for determining the associated risk of MS in case of positive extracranial ultrasonographic findings, by comparing the MS group with the control group using the approximation of Katz. P-Values up to 0.05 were considered statistically significant.
Recent studies have shown a significant association between MS and a newly recognized condition known as CCSVI. This condition is characterized by multiple stenoses of the principal pathways of the extracranial venous drainage, namely the internal jugular veins and the Azygus vein with the formation of collaterals to overcome intracranial hypertension. Moreover, hemodynamic impairment of intracranial circulation of MS patients has been confirmed by recently published data using magnetic resonance imaging (MRI) perfusion scans, susceptibility weighted images (SWI) and other advanced MRI sequences. Raised venous pressure and abnormal venous vasculature in MS patient with subsequent perivenous iron deposition has recently been described. Perivenous iron deposition around cerebral veins is a finding not widely accepted, but with initial documentation. Normally the blood leaves the brain by postural and respiratory mechanisms, where the venous outflow increases during inspiration. In the upright position cerebral venous outflow is through the vertebral veins, and in the supine position is via the internal jugular veins and the Azygus vein. Extracranial cerebrospinal venous outflow can be easily assessed with Color Doppler sonography which is a non-invasive technique.

Discussion

Figure 3.—Scan through the brachiocephalic vein (BCV) showing an echogenic flap (arrow).

Figure 4.—Schematic demonstration showing direction of blood flow in normal valve (A), in reversed one leaflet, (B) in thickened, transversely oriented one leaflet

Figure 5.—Ectatic carotid bulb (CB) indenting the internal jugular vein (IJV) causing narrowing and reflux.

Figure 6.—Distribution of abnormalities within the right and left IJVs in patients with multiple sclerosis.
and cost effective method. Intracranial venous hemodynamic assessment needs dedicated ultrasound setup 2, 5, 18, 20 which is not available in our Radiology Department.

Recently published studies have stated that there are several abnormalities observed in the intracranial and extracranial veins in MS patients which were not observed in patients with other neurodegenerative disorders nor in normal individuals. 1, 2, 3, 5 These abnormalities are known as Zamboni criteria, which include: 1) Reflux in the IJVs in sitting and supine posture; 2) Reflux in the DCVs; 3) High-resolution B-mode evidence of IJV stenoses; 4) Flow not Doppler-detectable in the IJVs. 5) Reverted postural control of the main cerebral venous outflow pathways. In the described criteria; we assumed the presence of at least two of the parameters in the same individual positive for evidence of CCSVI. 1, 2, 3 In our study, we observed that most MS patients have more than one positive criteria (84%), two patients were positive only for one criteria which was reflux with no definite morphological abnormalities, this could be explained by abnormal elasticity of the vein or due to a stenosis further distally or proximally 1, 2 which could not be detected by our equipment. The criteria that was common among the patients was persistent reflux in any body position (supine and/or sitting) for more than 0.88 seconds, which suggests that it may be due to a stenosis that cannot be changed with posture or respiratory mechanism rather than being as a result of valve incompetence. 1 In the healthy controls; 24% showed persistent reflux in the IJV for more than 0.88 seconds, but without the presence of any other criteria which is essential for the diagnosis of CCSVI. This finding was not observed in the Italian population, which may suggest some genetic or ethnic differences or predispositions in healthy people in Jordan for reflux that requires further investigations. However, the duration of reflux in MS patients was sustained for a longer duration than in controls, in some cases for seconds. We suggest that the definition of reflux as a variable in the diagnosis of CCSVI needs further evaluation. In two of the MS patients none of the criteria was seen, both patients were from the relapse remitting group of MS. This might be explained by the possibility of the presence of an abnormality elsewhere within the extracranial venous system, and requires further methods of investigation to estab-

lish the diagnosis of CCSVI, a bigger sample study should be performed to assess if this observation is more common than thought within the MS patients in the Jordanian population. Our results show that in the Jordanian population there is an increase risk of developing MS of more than 7 folds in patients with evidence of CCSVI (OR=7.2, 95% CI 2.9-18, P<0.0001). These results correlate well with the previously published and described data by Zamboni et al. which states that there is a strong significant association between the presence of CCSVI and MS. 1,4 The major drawback of this study is that it was non-blinded, although the ultrasound was performed and reported by two well trained radiologists, there is a possibility of bias knowing the patient from control. However, the findings were impressive, which warranted further larger double blinded multicenter trials.

Conclusions

In the Jordanian population; multiple sclerosis is strongly associated with hemodynamic abnormalities and morphological changes involving the Internal Jugular veins. These findings can be demonstrated by a non-invasive and cost effective Doppler ultrasound criteria.

References

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